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DETAILED DESCRIPTION

[Detailed Description of the Invention]

[0001]

[Industrial Application] this invention relates to the **** organization reproduction accelerator used in order to reproduce the **** organization destroyed by periodontitis etc.

[0002]

[Description of the Prior Art] Conventionally, the way a scaling etc. mainly removes a plaque is used as a cure for periodontitis, and when critical, **** surgery disposal is made. Although the chemotherapy by the antibiotic is tried recently, although these treatments are policies effective in preventing advance of periodontitis, they do not restore the destroyed **** organization positively and are not reproduced.

[0003] Although the periodontium has the structure where it does not see, in other organizations of adhering by firm combination of the fiber nature the hard tissue (root of tooth) and the tissue (gum) minded the periodontium, before a periodontium is reproduced, in order that the epithelial cell on the front face of gum may cover the pariodontal pocket with the conventional method (down growth of an epithelium), the epithelial tissue and a connective tissue normal between the roots of tooth cannot be reproduced, and a strong combination does not arise. For this reason, the reconstititution of the pariodontal pocket is carried out easily, as a result relapse of periodontitis and the regression of gum arise in high frequency.

[0004] On the other hand, the down growth of an epithelium is suppressed as a method of reproducing a normal fiber nature combination, with the radical-plane processing by (1) citric acid, and the high barrier film of (2) biocompatibility, and application ** to the part of the guidance anagenesis method (the GTR method) and (3) cell growth factors which secure the space for periodontium reproduction is proposed. However, since the method of (1) receives a cell, **** and the method of (2) have the trouble that the difference of the success percentage by the way person is large in order to arrange a barrier film by surgical disposal in the pariodontal-pocket section. Although the method of (3) has conquered (1) or (2) trouble, since it may give side effects other than a known operation to a living body by a lot of medication, it needs to give more effective medication conditions and needs to reduce the dose.

[0005] In view of such a situation, this invention person took lessons from the periodontium regenerant which was excellent in effectiveness, stability, and operability, and piled up research wholeheartedly.

[0006]

[Means for Solving the Problem] this invention offers the periodontium reproduction accelerator which comes to blend the cell growth factors which promote the regenerative function of the cell which constitutes the periodontium, and a tetracycline antibiotic into the same support.

[0007] Although the cell growth factor had the effect which reproduces the organization destroyed by gum disease also by independent medication, it was prescribing a tetracycline antibiotic for the patient simultaneously, and the activity of a cell growth factor was promoted and it found out that a multiplication-effect was acquired by the rebirth of the periodontium.

[0008] There are growth factors, such as a platelet origin cell growth factor, an epidermal growth factor, and a cell growth factor for insulins, among the growth factors used by this invention, especially a platelet origin cell growth factor is desirable. These growth factors are marketed from U.S. Gibco and U.S. Upstate Biotechnology, and can come to hand easily. These loadings have [ in a platelet origin cell growth factor and an epidermal growth factor ] 0.1 - 1 desirable % of the weight 0.01 to 0.1% of the weight at an insulin Mr. cell growth factor.

[0009] Moreover, in a tetracycline antibiotic, the minocycline and the doxycycline are desirable. These are marketed from U.S. Sigma and can come to hand easily. These loadings have 0.1 - 10 desirable % of the weight (potency).

[0010] the support by which this invention is permitted on physic according to a conventional method -- uniting -- pharmaceutical forms, such as gel and solution, -- it can carry out -- especially -- It excels in stability and is desirable when the support permitted on physic contains one or more sorts chosen from xanthan gum, a sodium alginate, and a carboxyvinyl polymer. 0.01 - 5.0 % of the weight of loadings is desirable.

[0011] In this way, the periodontium reproduction accelerator of this invention can be used by applying to the pariodontal pocket after **** surgery disposal or radical-plane **** disposal directly. Although it can fluctuate suitably by the symptom and part which should be treated, the desired periodontium reproduction effect is demonstrated with the dosage of 1 - 10micro of numbers g at once as an amount of peptides.

[0012]

[Example] The example of an experiment and an example are given to below, and this invention is explained to it in more detail.
[0013]
(Example 1 of prescription)
Platelet origin cell growth factor 1mg. The minocycline 1 g xanthan gum 1 g Energy Make Water ** **** Amount A 100 g (example 2 of prescription) platelet origin cell growth factor 1mg doxycycline 100 g(example 3 of prescription) <IBR> 1 g alginic-acid Na 0.5g energy Make Water ** **** Amount Epidermal growth factor . 1mg minocycline 1 g alginic-acid Na 1 g energy Make Water ** **** Amount A 100 g (example 4 of prescription) epidermal growth factor 1mg doxycycline 1 g carboxymethyl-cellulose 0.5 g energy Make Water ** **** Amount 100 g (example 5 of prescription) insulin Mr. cell growth factor 10mg doxycycline 1 g polyvinyl pyrrolidone 1 g energy Make water ** **** Amount 100 g (example 6 of prescription) insulin Mr. cell growth factor 10mg minocycline 1 g xanthan gum 0.5 g energy Make Water ** **** Amount 100 g (example 7 of prescription)
A platelet origin cell growth factor 1mg Minocycline 1 g carboxyvinyl polymer 1 g Energy Make Water ** **** Amount A 100 g (example 8 of prescription) platelet origin cell growth factor 1mg doxycycline 1 g carboxyvinyl polymer 0.5g energy Make Water ** **** Amount 100 g -- each It ****, a purified water is added and agitated and gel is **(ed).
[0014] As the gel of the examples 1, 3, 5, and 7 of example of examination (1) periodontium fiber blast cell multiplication activity test (method) prescription, and contrast. What blended only support by the antibiotic independent (contrast 1) (contrast 2), and the thing (contrast 3) blended by the cell growth factor independent were diluted with the same prescription 10,000 times to the Dulbecco strange method MEM (DMEM) culture medium which contains fetal calf serum 1%, and those proliferation-of-cells activity was measured. That is, it ****(ed) on the DIN tin block created from ****** of the cow which sterilized the periodontium fiber blast cell of the man origin, the after [ one week ] cell was exfoliated with the trypsin solution, and the number of cells was measured. A result is shown in Table 1.
[0015]
[Table 1]

| 検体 | | 細胞数(x10⁴個/1cm²) |
|---|---|---|
| 処方例1 | 対照1 | 3.3(100.0) |
| | 対照2 | 3.5(106.1) |
| | 対照3 | 4.7(142.4) |
| | 検体 | 5.9(178.8) |
| 処方例3 | 対照1 | 3.2(100.0) |
| | 対照2 | 3.3(103.1) |
| | 対照3 | 4.1(128.1) |
| | 検体 | 5.2(162.5) |
| 処方例5 | 対照1 | 3.8(100.0) |
| | 対照2 | 3.8(100.0) |
| | 対照3 | 4.1(107.9) |
| | 検体 | 5.0(131.6) |
| 処方例7 | 対照1 | 3.7(100.0) |
| | 対照2 | 3.8(102.7) |
| | 対照3 | 4.8(129.7) |
| | 検体 | 5.7(154.1) |

( ) 内は、各処方の対照1群を100とした値

The diluted solution of each prescription showed the promotion operation to multiplication of a periodontium fiber blast cell so that clearly from the result of Table 1.
[0016] (2) The pathological assay considered the operation of **** organization reproduction accelerator prescription various kinds to the **** organization renewal process after the operation (method) dog gum exfoliation **** operation to the **** organization renewal process after a dog gum exfoliation **** operation. According to the conventional method, the gum exfoliation **** operation was given to the vertical jaw premolar section which established the healthy **** organization by brushing etc. Under the present circumstances, in order to consider as the reference point of next histopathology-quantification, before and after deleting an alveolar bone, the reference point called notch to a radical plane was given. The sample prescribed for the patient the gel of the examples 1, 3, 5, and 7 of prescription shown in the example of prescription, and medicated the right-hand side vertical jaw with what blended only support by the antibiotic independent by the same prescription (contrast 1) (contrast 2), and the thing (contrast 3) blended by the cell growth factor independent as contrast. After the operation ****(ed) the gum valve and gave protection by a suture and the pack for one week. After evaluation extracted ******-ed week [ 4th ] after the operation and created the organization sample by the conventional method, it measured the distance between each part grades using the ocular micrometer under the microscope, and quantified it on the following criteria. A result is shown in Table 2.
[0017]
[Equation 1]

1：上皮のダウングロース率（%）

$$\frac{\text{骨削除前のノッチ下縁から上皮の再根尖側までの距離}}{\text{骨削除の長さ}} \times 100$$

2：線維性付着率（%）＝

$$\frac{\text{線維が垂直および斜走する部分の長さ}}{\text{骨削除の長さ}} \times 100$$

[0018]
[Table 2]

| 検体 | | 上皮のダウングロース率 | 線維性付着率 |
|---|---|---|---|
| 処方例1 | 対照1 | 10.6(100.0) | 33.7(100.0) |
| | 対照2 | 10.4(98.1) | 34.7(103.0) |
| | 対照3 | 10.2(96.2) | 39.2(116.3) |
| | 検体 | 9.5(89.6) | 41.7(123.7) |
| 処方例3 | 対照1 | 10.5(100.0) | 35.2(100.0) |
| | 対照2 | 10.3(98.1) | 35.3(103.1) |
| | 対照3 | 10.1(96.2) | 38.5(109.4) |
| | 検体 | 9.8(93.3) | 39.7(112.8) |
| 処方例5 | 対照1 | 10.8(100.0) | 33.8(100.0) |
| | 対照2 | 10.6(98.1) | 35.1(103.8) |
| | 対照3 | 10.4(96.3) | 38.6(114.2) |
| | 検体 | 9.9(91.7) | 40.7(120.4) |
| 処方例7 | 対照1 | 10.6(100.0) | 33.7(100.0) |
| | 対照2 | 10.2(96.2) | 34.0(100.9) |
| | 対照3 | 10.1(95.3) | 38.2(113.3) |
| | 検体 | 9.8(92.5) | 41.7(123.7) |

（）内は、各処方の対照1群を100とした値

As shown in Table 2, various prescription showed the promotion operation clearly to fiber nature deposit efficiency while suppressing the down growth of an epithelium.
[0019] 3) The histopathology-fixed quantity appraisal method considered the operation of a **** organization reproduction accelerator to the **** organization renewal process after the operation (method) ape gum exfoliation **** operation to the **** organization renewal process after an ape gum exfoliation **** operation. The gum exfoliation **** operation was given to the vertical jaw premolar section which established the healthy **** organization by brushing etc. according to the conventional method. Under the present circumstances, in order to consider as the reference point of next histopathology-quantification, before and after deleting an alveolar bone, the reference point called notch to a radical plane was given. The sample prescribed for the patient the gel of the examples 2, 4, 6, and 8 of prescription shown in the example of prescription, and medicated the right-hand side vertical jaw with what blended only support by the antibiotic independent by the same prescription (contrast 1) (contrast 2), and the thing (contrast 3) blended by the cell growth factor independent as contrast. After the operation ****(ed) the gum valve and gave protection by a suture and the pack for one week. After evaluation extracted [ postoperative 3 month ] ******-ed and created the organization sample by the conventional method, it measured the distance between each part grades using the ocular micrometer under the microscope, and quantified it on the following criteria. A result is shown in Table 3.
[0020]
[Equation 2]
新生セメント質の形成率(%)＝

$$\frac{\text{ノッチ下縁から新生セメント質の最歯冠側端までの距離}}{\text{セメントエナメル境からノッチ下縁までの距離}} \times 100$$

[0021]
[Table 3]

| 検体 | | 新生セメント質形成率(%) |
|---|---|---|
| 処方例2 | 対照1 | 23.3(100.0) |
| | 対照2 | 24.2(103.8) |
| | 対照3 | 26.7(114.5) |
| | 検体 | 29.4(124.5) |
| 処方例4 | 対照1 | 20.9(100.0) |
| | 対照2 | 21.3(101.9) |
| | 対照3 | 23.1(110.5) |
| | 検体 | 25.9(123.9) |
| 処方例6 | 対照1 | 23.4(100.0) |
| | 対照2 | 24.6(105.1) |
| | 対照3 | 26.0(111.1) |
| | 検体 | 28.1(120.1) |
| 処方例8 | 対照1 | 23.2(100.0) |
| | 対照2 | 24.1(103.8) |
| | 対照3 | 25.8(112.0) |
| | 検体 | 26.9(115.9) |

( ) 内は、各処方の対照1群を100とした値

As shown in Table 3, various prescription promoted formation of a new cement notably.

[0022]

[Effect of the Invention] According to this invention, the **** organization reproduction accelerator excellent in operability, stability, and effectiveness is obtained.

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[Translation done.]

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Time: 10:23:10

PALM INTRANET

# Inventor Information for 10/027669

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| Set | Items | Description |
|---|---|---|
| S1 | 6401 | POVIDONE |
| S2 | 863745 | BONE OR BMP??? OR OSTEO? |
| S3 | 187 | S1 AND S2 |
| S4 | 177 | S3 NOT (PY=2003 OR PY=2002 OR PY=2001 OR PC=US OR PC=EP OR PC=WO) |
| S5 | 168 | RD S4 (unique items) |

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| 2 | 43 | povidone same (bone or bmp$3 or osteo$) | USPAT; US-PGPUB | 2003/03/24 12:15 |
| 3 | 1 | us-6211157-$.did. | DERWENT | 2003/03/24 12:15 |

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| 2 | 6315 | (424/549;514/2,8;530/355).ccls. | USPAT; US-PGPUB; JPO; DERWENT | 2003/03/24 11:03 |
| 3 | 532 | (424/486;514/12,21,772.5;530/350,351,395,397,399).ccls. and @pd>20030223 | USPAT; US-PGPUB; JPO; DERWENT | 2003/03/24 11:22 |
| 4 | 76393 | pvp or vinyl adj pyrrolidone or vinylpyrrolidone or polyvinylpyrrolidone or povidone or pyrrolidinone | USPAT; US-PGPUB; JPO; DERWENT | 2003/03/24 11:20 |
| 5 | 968 | (((424/549;514/2,8;530/355).ccls.) or ((424/486;514/12,21,772.5;530/350,351,395,397,399).ccls. and @pd>20030223)) and (pvp or vinyl adj pyrrolidone or vinylpyrrolidone or polyvinylpyrrolidone or povidone or pyrrolidinone) | USPAT; US-PGPUB; JPO; DERWENT | 2003/03/24 11:05 |
| 6 | 50841 | growth adj factor or tgf$3 or bmp$3 or fgf$3 or igf$3 or egf$3 or hgf$3 or pdgf$3 | USPAT; US-PGPUB; JPO; DERWENT | 2003/03/24 11:06 |
| 7 | 554 | ((((424/549;514/2,8;530/355).ccls.) or ((424/486;514/12,21,772.5;530/350,351,395,397,399).ccls. and @pd>20030223)) and (pvp or vinyl adj pyrrolidone or vinylpyrrolidone or polyvinylpyrrolidone or povidone or pyrrolidinone)) and (growth adj factor or tgf$3 or bmp$3 or fgf$3 or igf$3 or egf$3 or hgf$3 or pdgf$3) | USPAT; US-PGPUB; JPO; DERWENT | 2003/03/24 11:06 |
| 8 | 8219 | vinyl adj pyrrolidone or polyvinylpyrrolidone or povidone or pyrrolidinone).clm. | USPAT; US-PGPUB; JPO; DERWENT | 2003/03/24 11:23 |
| 9 | 77 | (((424/549;514/2,8;530/355).ccls.) or ((424/486;514/12,21,772.5;530/350,351,395,397,399).ccls. and @pd>20030223)) and ((pvp or vinyl adj pyrrolidone or vinylpyrrolidone or polyvinylpyrrolidone or povidone or pyrrolidinone) adj polymer) | USPAT; US-PGPUB; JPO; DERWENT | 2003/03/24 11:07 |
| 10 | 6076 | (pvp or vinyl adj pyrrolidone or vinylpyrrolidone or polyvinylpyrrolidone or povidone or pyrrolidinone) with (lmw or mw or molecular adj weight or kda) | USPAT; US-PGPUB; JPO; DERWENT | 2003/03/24 11:21 |
| 11 | 6176 | (pvp or vinyl adj pyrrolidone or vinylpyrrolidone or polyvinylpyrrolidone or povidone or pyrrolidinone) with (lmw or mw or molecular adj weight or kda or da or dalton or kilodalton) | USPAT; US-PGPUB; JPO; DERWENT | 2003/03/24 11:21 |
| 12 | 21619 | (424/486,549;514/2,8,12,21,772.5;530/350,351,355,395,397,399).ccls. | USPAT; US-PGPUB; JPO; DERWENT | 2003/03/24 11:22 |
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| 14 | 122 | (((pvp or vinyl adj pyrrolidone or vinylpyrrolidone or polyvinylpyrrolidone or povidone or pyrrolidinone).clm.) and (((pvp or vinyl adj pyrrolidone or vinylpyrrolidone or polyvinylpyrrolidone or povidone or pyrrolidinone) with (lmw or mw or molecular adj weight or kda or da or dalton or kilodalton)) and ((424/486,549;514/2,8,12,21,772.5;530/350,351,355,395,397,399).ccls.)) | USPAT; US-PGPUB; JPO; DERWENT | 2003/03/24 11:23 |

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| 1 | 11 | (akella-rama$ or ranieri-john$).in. | USPAT; US-PGPUB | 2003/03/24 10:27 |

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